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- (i) a first polypeptide comprising a HECT E3 ubiquitin ligase WW domain; SEQ ID NO:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, or 13, or a variant thereof in which the ability of the polypeptide to bind to a Smad protein is not substantially diminished relative to the HECT E3 ubiquitin ligase;
- (ii) a second polypeptide comprising a Smad PY motif; SEQ ID NO:14, 15, 16, 17, 20, 21, 22, 23, 24, or 25, or a variant thereof in which the ability of the polypeptide to bind to an E3 ubiquitin ligase is not substantially diminished relative to a native Smad protein comprising the PY motif; and
- (iii) a candidate agent; under conditions that permit a detectable level of binding of the first polypeptide to the second polypeptide in the absence of candidate agent;

(b) determining a level of binding of the first polypeptide to the second polypeptide; and

(c) comparing the level of binding to a control level of binding of the first polypeptide to the second polypeptide in the absence of candidate agent, and therefrom determining whether the candidate agent modulates BMP-mediated signaling.

REMARKS

Claims 1-10 are pending. The Examiner objected to claim 1 for containing language encompassing a non-elected species of the invention. Claims 1 and 3-10 are rejected under 35 U.S.C. § 103(a) as being obvious over cited art. Claims 1-10 are rejected under 35 U.S.C. §112, first paragraph, for lack of enablement. Claims 1-10 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite. Claim 1 has been amended and is fully supported by the specification and claims as originally filed (*e.g.* page 10, the first full paragraph through page 15, the first paragraph). No new matter is introduced with these amendments.

Examiner's Objection to Claim 1

The Examiner objected to claim 1 for containing language encompassing a non-elected species of invention. Claim 1 has been amended to remove the language directed to the non-elected species. Specifically, “TGF- β - and/or” has been removed from the preamble and (c) of claim 1. Applicants respectfully submit that claim 1 is no longer directed to a non-elected species of the invention and the Examiner’s objection should be removed.